

REMARKS

Claims 69-75 and 82-99 are now pending in the present application (claims 1-68 and 76-81 having been canceled and new claims 82-99 having been added). Claims 69 and 75 have been amended. **Claim 69** has been amended to change the term "mammal" to "human;" to provide the full name of the gene referred to as NES1 (which appears in the specification at page 17, lines 14-15); and to remove reference to the sequence of the NES1 gene or to mutations thereof. Methods that include assessing the sequence of a human NES1 gene are now covered by new **claim 84** (and the claims that depend therefrom). **Claim 75** has been amended to remove the term "or activity." Any subject matter that is canceled is canceled without prejudice to Applicant's right to pursue that subject matter by way of a continuation application.

New dependent **claim 82** specifies additional sources of biological samples and is supported by the specification at, for example, page 10, lines 21-25. New **claim 83** is also supported by the specification at page 10 (*see* lines 15-19) and at page 36, lines 6-14. New **claims 85-88 and 93** are supported by, for example, original claims 25-30 and by the specification at page 10, lines 21-25. New **claims 89-92** further limit the method of claim 84 and are supported by the specification at, for example, page 35, lines 25-32. New **claim 95** is supported by the specification at, for example, page 36, lines 32-33. New **claims 94 and 99** specify the sequence of SEQ ID NO:2, which is the human NES1 nucleic acid sequence identified by Applicant (*see, e.g.,* Fig. 11).

New **claim 96** is very similar to previously pending claim 77 (*see also* page 3, lines 23-27). Applicant canceled claim 77 only to provide a more coherent claim set. Similarly, new **claim 97** corresponds to previously pending claim 78. New **claim 98** is supported by the specification at, for example, page 3, lines 23-27.

The specification has been amended to include sequence identifiers following the sequences that appear in the paragraph bridging pages 24 and 25 of the application.

No new matter has been added.

Objection to the Specification

The Examiner correctly points out that the application contains sequence disclosures that are encompassed by the definitions set forth in 37 CFR 1.821(a)(1) and (a)(2). Accordingly, Applicant has inserted sequence identifiers into the application where appropriate.

Obviousness-type Double Patenting

The Examiner rejected claims 69-78 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 and 11-14 of U.S. Patent No. 6,153,387.

Should the Examiner remain persuaded that the claims of the present application are not patentably distinct (from those of U.S. Patent No. 6,153,387) when otherwise in condition for allowance, Applicant will file a terminal disclaimer.

35 U.S.C. § 112, ¶ 1

Claims 69-78 were rejected "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (Office action at page 4). More specifically, the Examiner states that the specification "only provides a single representative species from human cell lines, i.e., the NES1 gene of SEQ ID NO:2" and that, given the "lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently described the claimed invention" (Office action at page 4).

In view of the amendment of claim 69, this ground for rejection should be withdrawn. Claim 69 now covers a method of determining whether a human – not any mammal, but only a human – has a carcinoma or an increased likelihood of developing a carcinoma. Moreover, to fall within the claim, one must examine the expression of a NES1 gene *in a biological sample obtained from the human*. As the Examiner notes, Applicant has disclosed the sequence of the NES1 gene from *human* cells (SEQ ID NO:2). As Applicant has disclosed the sequence of the

human NES1 gene, and as the present claims are limited to a diagnostic method that relies on assessing expression of the NES1 gene in human tissue, the written description is commensurate with the scope of the claims. Applicant's disclosure has reasonably conveyed, to one of ordinary skill in the art, that Applicant was in possession of the method now claimed.

New independent claims 84 and 95 similarly use the term "human" rather than "mammal."

With respect to claim 75 (specifically addressed at page 4 of the Office action), the Examiner is asked to note the amendment in which the phrase "or activity" has been deleted.

Claims 69-78 were also rejected "as the disclosure is enabling only for claims limited to NES1 gene of SEQ ID NO:2 from human" (Office action at page 4). The Examiner states that the "claims are broader than the enablement provided by the disclosure with regard to the large number of all possible NES1 genes [*sic.*] from any mammal" (Office action at pages 4-5). Other statements also focus on Applicant's use of the term "mammal." For example, the Examiner states (Office action at page 4; emphasis added):

The nature and breadth of the claimed invention encompasses any composition comprising a gene encoding NES1 polypeptide from *any mammalian source* ...

While molecular biological techniques and genetic manipulation to make the protein of SEQ ID NO:1 are known ... knowledge regarding *all types* of NES1 proteins ... is lacking.

Thus, searching for a NES1 gene which is down regulated due to *any mammalian cell transformation* which may or may not have a serine protease activity and/or mutants [*sic.*] thereof is well outside the realm of routine experimentation ...

In view of the present amendment, this ground for rejection should also be withdrawn. As noted above, Applicant has clearly disclosed the sequence of a human NES1 gene as well as studies, conducted with human cell lines, that led to the conclusion that "NES1 mRNA expression appears to be down-regulated during tumorigenic progression and not by mere immortalization of mammary cell" (specification at page 20, lines 18-20). Thus, Applicant provided a complete target sequence, and methods of assessing gene expression are routinely

carried out by those of ordinary skill in the art. As Applicant's claims (see amended claim 69 and the claims that depend therefrom) now cover methods of determining whether a *human* has a carcinoma or an increased likelihood of developing a carcinoma by examining the expression of a NES1 gene in a biological sample obtained *from the human* (*i.e.*, by assessing the human gene in the human sample), there is unlikely to be any need for experimentation, let alone experimentation that is undue.

New independent claim 84 and the claims that depend therefrom (85-95) cover methods that are similar to those covered by claims 69-83 except they require one to assess the sequence of the human NES1 sequence rather than its level of expression. Applicant's specification teaches that mutations in the NES1 sequence can result in a loss of gene expression. Thus, Applicant disclosed, and now claims, methods of determining whether a human has a carcinoma, or an increased risk of developing a carcinoma, by assessing the sequence of a human NES1 gene. Here again, Applicant provided the target sequence, and methods of assessing a sequence to identify a mutation are routinely carried out by those of ordinary skill in the art. Applicant has met the legal standards for patentability with respect to the method of claim 84: one of ordinary skill in the art would find that Applicant was in possession of that method and would be able to carry out the method without resort to undue experimentation.

35 U.S.C. § 112, ¶ 2

Claims 69-78 were rejected as being indefinite (Office action at page 5). More specifically, the Examiner states that "claims 69, 74, 75, 77, and 78 contain the undefined abbreviation NES1" and that "[t]he term NES1 could either refer to the oligopeptide of SEQ ID NO:1 or any other serine [*sic.*] protease that is expressed in normal mammalian cells but not in transformed tumor cells" (Office action at page 6).

In view of the amendment of claim 69, this ground for rejection should now be withdrawn. Applicant has amended claim 69 to specify that the abbreviation NES1 representation Normal Epithelial Specific-1 and that the NES1 gene whose expression is assessed is a human NES1 gene.

The Examiner further states that the phrase "NES1 protein ... or activity" renders the claims indefinite, and that the "specification does not define NES1 protein activity and one of ordinary skill in the art would not [know] what it is" (Office action at page 6).

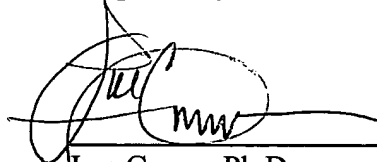
Applicant has removed the term "or activity" from the claims. Accordingly, this ground for rejection should also be withdrawn.

CONCLUDING REMARKS

Enclosed is a check for \$475 in payment of the Petition for Extension of Time fee.
Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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Lee Crews, Ph.D.
Reg. No. 43,567

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906